AMENDMENTS TO THE CLAIMS

Please kindly amend the claims as follows:

1. (Original) A method of modifying a producer cell which producer cell comprises integrated into its genome a provirus which provirus comprises one or more recombinase recognition sequences within or upstream of its 3' LTR, the method comprising:

introducing into the cell a construct comprising a 5' recombinase recognition sequence, an LTR and a 3' recombinase recognition sequence in that order, in the presence of a recombinase which is capable of acting on the recombinase recognition site(s) such that the nucleotide sequence between the 5' and 3' recombinase recognition sequences in the construct is introduced into the provirus.

2. (Original) A method according to claim 1 wherein the construct further comprises at least one nucleotide sequence of interest (NOI) between the 5' recombinase recognition sequence and the LTR, which NOI is operably lined to a transcriptional regulatory sequence.

3. (Previously amended) A method according to claim 1, wherein the construct further comprises the 5' LTR and/or the packaging signal.

4. (Previously amended) A method according to claim 1, wherein the construct LTR is a heterologous regulatable LTR.

5. (original) A method according to claim 4 wherein the regulatable LTR comprises an ischaemic like response element (ILRE).

6. (Previously amended) A method according to claim 1, wherein the construct LTR is inactive.

7. (Previously amended) A method according to claim 1, wherein the provirus comprises an NOI encoding a selectable marker, which NOI is flanked by recombinase recognition sites.

8. (Previously amended) A method according to claim 1, wherein the provirus comprises an internal 5' LTR upstream of the recombinase site or the 5' recombinase site where there is more than one site.

9. (Currently amended) A method according to ~~any one of the preceding claims~~ claim 8 wherein the U3 region of the 5' LTR is inactive.

10. (Previously amended) A method according to claim 1, wherein the U3 region of the 5' LTR and/or the U3 region of the second internal 5' LTR comprises a heterologous promoter.

11. (Previously amended) A method according to claim 1, wherein the provirus comprises two recombinase recognition sites and as a preliminary step, the recombinase is expressed in a host cell such that the nucleotide sequence present between the two sites is excised.

12. (Previously amended) A method according to claim 1, wherein the producer cell is a high titre producer cell, capable of producing at least 10^6 retrovirus particles per ml.

13. (Previously amended) A method according to claim 1, wherein the provirus is a lentivirus.

14. (Original) A method according to claim 13, wherein the lentivirus is HIV or EIAV.

15. (Previously amended) A method according to claim 2, wherein the provirus further comprises a second NOI.

16. (Previously amended) A producer cell obtainable by the method of claim 1.

17. (Original) An infectious retroviral particle obtainable from the producer cell of claim 16.

18. (Currently amended) A derived producer cell, obtained by the method of claim 1, said cell comprising integrated into its genome a retroviral vector comprising in the 5' to 3' direction a first 5' LTR; a second NOI operably lined to a second regulatable 3' LTR; and a third 3' LTR;

wherein the third LTR is positioned downstream of the second LTR in the producer cell.

19. (Original) A producer cell according to claim 18 wherein the first 5' LTR comprising 5'R and 5' U5 sequences is derivable from a first vector; the second NOI operably linked to a second regulatable 3' LTR is derivable from a second vector; and the third 3' LTR is derivable from the first vector.

20. (Currently amended) A producer cell according to claim [~~18 or~~] 19 wherein the first vector comprises a retroviral vector wherein the retroviral vector comprises a first NOI flanked by recombinase recognition sequences.

21. (Currently amended) A producer cell according to claim [~~19 or~~] 20 wherein the retroviral vector further comprises an internal LTR located upstream of the first NOI and downstream of a packaging signal wherein the internal LTR comprises a heterologous U3 sequence linked to heterologous R and U5 sequences.

22. (Currently amended) A producer cell according to claim 18, wherein the third LTR is transcriptionally ~~quiscent~~ quiescent.

23. (Currently amended) A producer cell according to claim 22, wherein the third [~~3'~~] LTR comprises a deletion in the U3 sequence.

24. (Previously amended) A producer cell according to claim 20, wherein the first NOI is a selectable marker.

25. (Original) A producer cell according to claim 19 wherein the second vector comprises a second NOI operably linked to a second regulatable 3'LTR comprising at least on recombinase recognition sequence.

26. (Previously amended) A producer cell according to claim 25, wherein the second LTR comprises a deletion in the U3 sequences in the 3' LTR.

27. (Previously amended) A producer cell according to claim 25, wherein the second NOI comprises a coding sequence operably linked to a promoter.

28. (Previously amended) A producer cell according to claim 20, wherein the first NOI is a selectable marker.

29. (Original) A producer cell according to claim 28 wherein the dicistronic construct comprises a therapeutic gene, an internal ribosomal entry site (IRES) and a reporter gene.

30. (Previously amended) A method for producing a high titre regulatable retroviral vector, the method comprising:

(i) providing a derived producer cell comprising integrated into its genome a first vector;

(ii) introducing a second vector into the derived producer cell using a recombinase assisted method;

wherein the derived producer cell comprises a retroviral vector comprising in the 5' to 3' direction a first LTR (5' LTR); a second NOI operably linked to a second LTR (regulatable 3' LTR); and a third LTR (3' LTR); wherein the third LTR is positioned downstream of the second LTR in the derived producer cell.

31. (Original) A method according to claim 30 wherein the third 3' LTR is transcriptionally active but expression is directed away from the second regulatable 3'LTR.

32. (Original) A method for introducing a second regulatable 3'LTR into a derived producer cell wherein the method comprises a recombinase assisted method.

33. (Original) A method according to claim 32 wherein the recombinase assisted method is a Cre/lox recombinase method.

34. (Previously amended) A process for preparing a regulated retroviral vector, comprising performing the method according to claim 30 and preparing a quantity of the regulated retroviral vector.

35. (Original) A regulated retroviral vector produced by the process according to claim 34.

36. (Original) A regulated retroviral vector according to claim 35 wherein the retroviral vector is capable of transducing a target site.

37. (Original) A regulated retroviral vector according to claim 36 wherein the retroviral vector is produced in sufficient amounts to effectively transducer a target site.

38. (Previously amended) A regulated retroviral vector according to claim 36 wherein the target site is a cell.

39. (Original) A cell transduced with a regulated retroviral vector according to claim 38.

40. (Previously amended) A regulated retroviral vector according to claim 35 in combination with a pharmaceutically acceptable carrier.

41. (Previously amended) A medicament for diagnostic and/or therapeutic and/or medical applications, comprising a regulated retroviral vector according to claim 35.

42. (canceled)

43. (Previously amended) A derived stable producer cell capable of expressing regulated retroviral vectors according to claim 35.

44. (Original) A derived stable producer cell according to claim 43 wherein the regulated retroviral vector is a high titre regulated retroviral vector.

45. (canceled)

46. (canceled)

47. (canceled) A nucleic acid vector according to claim 45, further comprising a 5' LTR and/or a packaging signal.

48. (canceled) A nucleic acid vector according to claim 45, wherein the LTR is a heterologous regulatable LTR.

49. (canceled) A nucleic acid vector according to claim 45, wherein the LTR is transcriptionally quiscent.

50. (New) A nucleic acid vector comprising a 5' recombinase recognition sequence, a regulatable LTR and a 3' recombinase recognition sequence in that order.

51. (New) A nucleic acid vector according to claim 50 further comprising at least one NOI between the 5' recombinase recognition sequence and the regulatable LTR.

52. (New) A nucleic acid vector according to claim 50, further comprising a 5' LTR and/or a packaging signal.

53. (New) A nucleic acid vector according to claim 50, wherein the LTR is a heterologous regulatable LTR.

54. (New) A nucleic acid vector according to claim 50, wherein the LTR is transcriptionally quiescent.